Osteoarthritis | degenerative joint disease

OVERVIEW
- Articular cartilage deterioration + compensatory bone changes
- Chronic, non-inflammatory
- Clinical events: cartilage destruction, joint space narrowing, sclerosis, osteophyte spur formation
- Risk factors: age, female, obesity, poor quad strength, trauma, repetitive activities, genetic factors (type II cartilage abnormalities)

CLASSIFICATION
- **Primary OA**: idiopathic
  - Localized: 1 or 2 sites
  - Generalized: ≥3 sites
  - Erosive: erosion & marked proliferation of proximal & DIP joints of hands
- **Secondary OA**: associated with RA, trauma, metabolic, or endocrine disorders

PATHOPHYSIOLOGY
- Cartilage degradation → thinner + cracks in cartilage → gaps expand → gaps reach bone → synovial fluid leaks into cracks → further damage + cysts + deformities
- Major players: MMP, collagen II, PG, GAGs
- Effects on bone: denudation, eburnation, osteoids

CLINICAL PRESENTATION
- Clinical features: pain, swelling, crepitus, contracture of joint, deformity, altered gait
- Symptoms: pain, joint stiffness after inactivity, crepitus on motion, limited joint motion, bony joint enlargement
- Signs: no specific lab abnormalities
- Radiographic evidence: may be present without symptoms
  - Early mild OA: radiographic changes often absent
  - Progression of OA: joint space narrowing, subchondral bone sclerosis, marginal osteophytes
  - Late OA: abnormal joint alignment, effusions in joint spaces

NON-PHARMACOLOGIC THERAPY
Patient education, strengthening & range-of-motion exercises, rest, physical therapy, dietary modifications, assistive devices, joint protection, weight loss, joint replacement surgery

PHARMACOLOGIC TREATMENT
General approach to treatment
- **1st line**: APAP (max 4g/day), topical capsaicin, consider glucosamine & chondroitin
  - Acetaminophen
    - MOA: (-)COX → (-)PG synthesis
    - P'kinetics: well absorbed, peaks in 1-2hrs, hepatic metabolism, renally excreted
    - Interactions: isoniazid
    - Dose: max 4g/day
- **2nd line**: NSAIDs/COX2 inhibitors, another NSAID if first one inadequate
- **Alternatives**: methyl salicylate (Bengay), hyaluronic injection, corticosteroid injection, narcotics, tramadol

Comparable relief

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
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<tbody>
<tr>
<td>APAP</td>
<td>2.6-4 g/day</td>
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<tr>
<td>ASA</td>
<td>650 mg qid</td>
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<tr>
<td>IBU</td>
<td>1200-2400 mg/day</td>
</tr>
<tr>
<td>Naproxen</td>
<td>750 mg/day</td>
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NSAIDs
- Effects: anti-inflammatory, analgesic, antipyretic, palliative purposes only
- Onset of effect: pain 1-2hrs, fever ½-2hrs, inflammation 2-3 weeks
- No hepatic metabolism: sulindac, nabumetone
- Compared to ASA: ↑ efficacy, ↓ GI effects, ↑ $, reversible inhibition of platelets
- Common SE: GI, ototoxicity, cutaneous, dizziness
- Risks with long-term use: ulcerations, bleeding, perforations, obstructions
- Renal complications: peripheral edema, transient acute renal insufficiency, tubulointerstitial nephropathy, hyperkalemia, renal papillary necrosis
  - Etiology: (–) prostaglandins affects intrarenal blood flow
  - Patients at risk: CHF, cirrhosis, ascites, volume contraction, age, nephrotoxic drugs
  - Clinical findings: ↑ SCR, ↑ BUN, ↑ K⁺, peripheral edema, ↑ weight
- Lung complications: airway edema, bronchoconstriction, inflammation
  - Etiology: (–) COX funnels substrates down LOX pathway
  - Patients at risk: asthmatics
- Interactions: ↑ effect (Li⁺, warfarin, MXT) & ↓ effects (ACEI, β blockers, diuretics)

COX-2 inhibitors
- Available agents: celecoxib, rofecoxib, valdecoxib, meloxicam
- Contraindications: (same as other NSAIDs) ASA allergy, NSAID allergy, renal risk, liver risk
  - Celecoxib: sulfa allergy
- Interactions: drugs that (–) CYP2C9 may ↑ AUC of celecoxib, e.g. fluconazole
  - Others: Li⁺, ACEI, furosemide
  - Aspirin, warfarin: ↑ risk of GI ulceration and bleeding
- ↑ CV risk: exact mechanism unknown
  - Unopposed TXA2 production → imbalance between COX1 & COX2 prostaglandins due to COX2 selectivity → ↑ prothrombotic state
  - (–) COX2 → ↓ prostacyclin protective mechanisms → vasoconstriction, Na & H₂O retention → ↑ bp → edema, HF exacerbation
  - Diclofenac (similar to rofecoxib) associated with substantial CV risk because more COX2 selective, even topical gel holds risks
  - Naproxen associated with least CV risk

TOPICAL MEDICATIONS

Topical NSAIDs
- 1% diclofenac gel
  - Indication: osteoarthritis in hands and knees
  - SE: application site reactions, CV risks, allergies, hepatotoxicity
  - Dose: 4g applied to lower extremities qid, 2g to upper extremities qid
- 1% diclofenac solution: 40 drops spread around affected knee qid

Topical capsaicin
- Indication: 1st line for pain in specific joints
- MOA: (+) substance P release → neuronal depletion
- Dose: applied qid → tid or bid after 1 month
- Advantages: ↓ systemic absorption, OTC, treats affected joints, can use in combo
- Disadvantages: frequent application, delayed efficacy with immediate application site side effects, cost

Others topicals: methylsalicylate (Bengay), menthol/phenol/camphor
INTRA-ARTICULAR INJECTIONS

Intra-articular injections: corticosteroids
- **Indication**: 2nd line for pain in specific joints, 1st line for pain in specific joints with effusion
- **Dose**: 10-20mg triamcinolone hexacetonide or 20-40mg methylprednisolone acetate
- **Advantages**: quick relief (1-2 days), no interactions, can remove liquid
- **Disadvantages**: temporary relief only, limit 3-4 times/year per joint due to potential cartilage damage

Intra-articular injections: hyaluronic acid
- **Indication**: OA of knee in non-responders (not for hip)
- **MOA**: joint lubricant
- **Dose**: joint & drug dependent
- **Advantages**: longer relief compared to steroids, no interactions, can remove fluid
- **Disadvantages**: longer to get relief, temporary/short-lived relief only

SUPPLEMENTS

Dietary supplements: glucosamine & chondroitin
- **Indication**: mild-moderate disease
- **MOA**: GAG? Unknown
- **Dose**: glucosamine 1500mg daily + chondroitin 1200mg daily
- **Advantages**: OTC
- **Disadvantages**: conflicting data on efficacy and quality

OTHER ALTERNATIVE TREATMENT

Tramadol
- **MOA (dual)**: mu-opioid receptor, (-)NE & 5-HT reuptake
- **Advantages**: no GI bleed
- **Disadvantages**: questionable efficacy in OA, lack anti-inflammatory effects, tolerance
  - Contraindication: opioid hypersensitivity

Narcotic analgesics (codeine, oxycodone)
- **Indication**: only if other treatments ineffective or intolerable
- **Dose**: lowest effective dose
- **Place in therapy**: in conjunction with non-pharmacological therapy, for short term use only